

CLAIM AMENDMENTS:

1. (Currently Amended) A microparticle ~~having an adsorbent surface, said microparticle comprising:~~

a biodegradable polymer, selected from the group consisting of a poly(α -hydroxy acid), a polyhydroxy butyric acid, a polycaprolactone, a polyorthoester, a polyanhydride, and a polycyanoacrylate; and

a detergent selected from a cationic detergent and an anionic detergent; and

an immunological adjuvant, wherein said immunological adjuvant is adsorbed on the surface of said microparticle.

2. (Currently Amended) The microparticle of claim 1, further comprising an antigen derived from a pathogenic organism or a tumor, wherein said antigen is adsorbed on the surface of said microparticle, encapsulated within said microparticle, or both. further comprising a first biologically active macromolecule adsorbed on the surface thereof, wherein the first biologically active macromolecule is at least one member selected from the group consisting of a polypeptide, a polynucleotide, a polynucleoside, an antigen, a pharmaceutical, a hormone, an enzyme, a transcription or translation mediator, an intermediate in a metabolic pathway, an immunomodulator, and an adjuvant.

3. (Currently Amended) The microparticle of claim ~~2~~ 1, wherein the biodegradable polymer is selected from the group consisting of a poly(α -hydroxy acid), a polyhydroxy butyric acid, a polycaprolactone, a polyorthoester, a polyanhydride, and a polycyanoacrylate. further comprising a second biologically active macromolecule encapsulated within said microparticle, wherein the second biologically active macromolecule is at least one member selected from the group consisting of a polypeptide, a polynucleotide, a polynucleoside, an antigen, a pharmaceutical, a hormone, an enzyme, a transcription or translation mediator, an intermediate in a metabolic pathway, an immunomodulator, and an adjuvant.

4. (Currently Amended) The microparticle of ~~any of claims 1-3~~ claim 1, wherein the microparticle comprises a poly(α -hydroxy acid) selected from the group consisting of poly(L-lactide), poly(D,L-lactide) and poly(D,L-lactide-co-glycolide).

5. Cancelled.

6. (Currently Amended) The microparticle of ~~any of claims 1-5~~ claim 1, wherein the microparticle comprises detergent is a cationic detergent.

7. (Currently Amended) The microparticle of ~~any of claims 1-5~~ claim 1, wherein the microparticle comprises detergent is an anionic detergent.

8. (Currently Amended) The microparticle of ~~any of claims 1-5~~ claim 2, wherein the antigen is an antigen comprising a polypeptide. ~~detergent is a nonionic detergent.~~

9. (Currently Amended) The microparticle of ~~any of claims 2-8~~ claim 2, wherein the antigen is an antigen comprising a polynucleotide. ~~first biologically active macromolecule is an antigen selected from the group consisting of gp120, p24gag, p55gag, and Influenza A hemagglutinin antigen.~~

10. Cancelled.

11. (Currently Amended) The microparticle of ~~any of claims 3-10~~ claim 1, wherein the microparticle further comprises an immunological adjuvant encapsulated within the microparticle. ~~second biologically active macromolecule is an adjuvant.~~

12. (Currently Amended) The microparticle of ~~any of claims 1-11~~ claim 1, wherein the immunological adjuvant is selected from a CpG oligonucleotide, an E. coli heat-labile toxin, a monophosphorylipid A compound, and an aluminum salt.

13. (Currently Amended) The microparticle of claim 2, wherein the microparticle comprises a cationic detergent. A microparticle composition comprising a microparticle of any of claims 1-12 and a pharmaceutically acceptable excipient.

14. (Currently Amended) The microparticle of claim 2, wherein the microparticle comprises an anionic detergent. A microparticle composition comprising a microparticle according to any of claims 1-13, further comprising an adjuvant.

15. Cancelled.

16. Cancelled.

17. (Currently Amended) A method of producing a microparticle ~~having an adsorbent surface,~~ said method comprising the steps of:

(a) providing an emulsion dispersing a mixture comprising (i) an organic solvent, (ii) a biodegradable polymer, (iii) water and (iv) a detergent selected from a cationic detergent and an anionic detergent, of a polymer solution and a detergent, wherein the polymer solution comprises a polymer selected from the group consisting of a poly(α -hydroxy acid), a polyhydroxy butyric acid, a polycaprolactone, a polyorthoester, a polyanhydride, and a polycyanacrylate, wherein the polymer is present at a concentration of about 1% to about 30% relative to the in an organic solvent, and wherein the detergent is present in the mixture at a weight to weight detergent to polymer ratio of from about 0.00001:1 to about 0.1:1; and

(b) removing the organic solvent from the emulsion; and

(c) adsorbing an immunological adjuvant on the surface of said microparticle.

18. (Currently Amended) The method of claim 17 wherein the detergent comprises ~~is an~~ anionic detergent.

19. (Currently Amended) The method of claim 17 wherein the detergent comprises ~~is a~~ cationic detergent.

20. (Currently Amended) The method of claim 17 wherein the detergent further comprises is a nonionic detergent.

21. (Currently Amended) The method of ~~any of claims 17-20~~ claim 17 wherein the detergent is present at a weight to weight detergent to polymer ratio of from about 0.0001:1 to about ~~0.01:1~~ 0.1:1.

22. (Currently Amended) The method of ~~any of claims 17-20~~ claim 17 wherein the detergent is present at a weight to weight detergent to polymer ratio of from about 0.001:1 to about ~~0.01:1~~ 0.1:1.

23. (Currently Amended) The method of ~~any of claims 17-20~~ claim 17 wherein the biodegradable polymer comprises a poly(α -hydroxy acid), a polyhydroxy butyric acid, a polycaprolactone, a polyorthoester, a polyanhydride, or a polycyanoacrylate. detergent is present at a weight to weight detergent to polymer ratio of from about 0.005:1 to about 0.01:1.

24. (Currently Amended) The method of ~~any of claims 17-23~~ claim 17, wherein the biodegradable polymer microparticle comprises a poly(α -hydroxy acid) selected from the group consisting of poly(L-lactide), poly(D,L-lactide) and poly(D,L-lactide-co-glycolide).

25. (Currently Amended) The method of ~~claim 24~~ claim 17, wherein the ~~microparticle comprises poly(D,L-lactide-co-glycolide)~~ biodegradable polymer comprises poly(lactide-co-glycolide).

26. (Currently Amended) The method of ~~claim 25~~ claim 17, wherein the biodegradable polymer microparticle comprises poly(D,L-lactide-co-glycolide) and is present at a concentration of about 3% to about 10% relative to the organic solvent.

27. Cancelled.

28. (Currently Amended) The method of claim 17, wherein said emulsion is a water-in-oil-in-water emulsion. 27, wherein the macromolecule is at least one member selected from the group

~~consisting of a pharmaceutical, a polynucleotide, a polynucleoside, a polypeptide, a hormone, an enzyme, a transcription or translation mediator, an intermediate in a metabolic pathway, an immunomodulator, an antigen, and an adjuvant.~~

29. (Currently Amended) The method of claim 17, further comprising providing an antigen derived from a pathogenic organism or a tumor, wherein said antigen is adsorbed on the surface of said microparticle, encapsulated within said microparticle, or both. ~~any of claims 27-28, wherein the macromolecule is an antigen selected from the group consisting of gp120, p24gag, p55gag and Influenza A hemagglutinin antigen.~~

30. (Currently Amended) The method of claim 29, wherein the antigen is adsorbed on the surface of said microparticle. ~~29, wherein the macromolecule is a polynucleotide which encodes gp120.~~

31. (Currently Amended) The method of claim 29, wherein the antigen is an antigen comprising a polynucleotide. ~~any of claims 27-30 wherein the detergent is present at a weight to weight detergent to polymer ratio of from about 0.0001:1 to about 0.01:1.~~

32. (Currently Amended) The method of claim 29, wherein the antigen is an antigen comprising a polypeptide. ~~any of claims 27-30 wherein the detergent is present at a weight to weight detergent to polymer ratio of from about 0.001:1 to about 0.01:1.~~

33. (Currently Amended) The method of claim 17, further comprising providing an immunological adjuvant within the microparticle. ~~any of claims 27-30 wherein the detergent is present at a weight to weight detergent to polymer ratio of from about 0.005:1 to about 0.01:1.~~

34. (Currently Amended) A microparticle made according to the method of any of claims 17-26 and 28-33.

35. (Original) A microparticle composition comprising a microparticle of claim 34 and a pharmaceutically acceptable excipient.

36. Cancelled.

37. Cancelled.

38. (Currently Amended) A method of delivering a therapeutically effective amount of a ~~macromolecule~~ an immunological adjuvant to a vertebrate subject comprising the step of administering to the vertebrate subject a microparticle composition of claim 35. ~~any of claims 13-16, 35, or 37.~~

39. Cancelled.

40. (Currently Amended) Use of a microparticle composition ~~of any of claims 13-16, 35, or 37~~ claim 35 for treatment of a disease.

41. (Currently Amended) Use of a microparticle composition ~~of any of claims 13-16, 35, or 37~~ claim 35 for a vaccine.

42. (Currently Amended) Use of a microparticle composition ~~of any of claims 13-16, 35, or 37~~ claim 35 for raising an immune response.

43. Cancelled.

44. Cancelled.

45. Cancelled.

46. Cancelled.

47. Cancelled.

48. Cancelled.

49. Cancelled.

50. Cancelled.

51. Cancelled.

52. (Newly added) The microparticle of claim 6, wherein said immunological adjuvant comprises an immunostimulating nucleotide sequence.

53. (Newly added) The microparticle of claim 52, wherein the immunological adjuvant comprises a CpG oligonucleotide.

54. (Newly added) The microparticle of claim 13, wherein the antigen (a) is adsorbed on the surface of the microparticle and (b) comprises a polynucleotide.

55. (Newly added) The microparticle of claim 14, wherein the antigen (a) is adsorbed on the surface of the microparticle and (b) comprises a polypeptide.

56. (Newly added) The microparticle of claim 2, wherein said antigen is selected from HIV antigens, hepatitis B virus antigens, hepatitis C virus antigens, *Haemophilus influenza* type B antigens, meningitis B antigens, pertussis antigens, diphtheria antigens, tetanus antigens and influenza A virus antigens.

57. (Newly added) The microparticle of claim 2, wherein the antigen comprises a plasmid DNA molecule.

58. (Newly added) The microparticle of any of claims 1-4, 6-9, 11-14 and 52-57, wherein the microparticle has a diameter between 500 nanometers and 30 microns.

59. (Newly added) The microparticle of any of claims 1, 2, 6-9, 11-14 and 52-57, wherein the microparticle comprises poly(lactide-co-glycolide).
60. (Newly added) The microparticle of any of claims 3, 4, 8, 11, 12 and 56, wherein the microparticle comprises an anionic detergent.
61. (Newly added) The microparticle of any of claims 3, 4, 9, 11, 12, 56 and 57, wherein the microparticle comprises a cationic detergent.
62. (Newly added) A microparticle composition comprising a microparticle of any of claims 1-4, 6-9, 11-14 and 52-57, and a pharmaceutically acceptable excipient.
63. (Newly added) The microparticle composition claim 62, wherein said microparticle composition is an injectable composition.
64. (Newly added) A method of delivering a therapeutically effective amount of an immunological adjuvant to a vertebrate subject comprising the step of administering to the vertebrate subject a microparticle composition of claim 62.
65. (Newly added) Use of a microparticle composition of claim 62 for treatment of a disease.
66. (Newly added) Use of a microparticle composition of claim 62 for a vaccine.
67. (Newly added) Use of a microparticle composition of claim 62 for raising an immune response.
68. (Newly added) A microparticle composition comprising a microparticle of claim 58 and a pharmaceutically acceptable excipient.
69. (Newly added) The microparticle composition claim 68, wherein said microparticle composition is an injectable composition.

70. (Newly added) A method of delivering a therapeutically effective amount of an immunological adjuvant to a vertebrate subject comprising the step of administering to the vertebrate subject a microparticle composition of claim 68.
71. (Newly added) Use of a microparticle composition of claim 68 for treatment of a disease.
72. (Newly added) Use of a microparticle composition of claim 68 for a vaccine.
73. (Newly added) Use of a microparticle composition of claim 68 for raising an immune response.
74. (Newly added) A microparticle composition comprising a microparticle of claim 59 and a pharmaceutically acceptable excipient.
75. (Newly added) The microparticle composition claim 74, wherein said microparticle composition is an injectable composition.
76. (Newly added) A method of delivering a therapeutically effective amount of an immunological adjuvant to a vertebrate subject comprising the step of administering to the vertebrate subject a microparticle composition of claim 74.
77. (Newly added) Use of a microparticle composition of claim 74 for treatment of a disease.
78. (Newly added) Use of a microparticle composition of claim 74 for a vaccine.
79. (Newly added) Use of a microparticle composition of claim 74 for raising an immune response.
80. (Newly added) A microparticle composition comprising a microparticle of claim 60 and a pharmaceutically acceptable excipient.

81. (Newly added) The microparticle composition claim 80, wherein said microparticle composition is an injectable composition.
82. (Newly added) A method of delivering a therapeutically effective amount of an immunological adjuvant to a vertebrate subject comprising the step of administering to the vertebrate subject a microparticle composition of claim 80.
83. (Newly added) Use of a microparticle composition of claim 80 for treatment of a disease.
84. (Newly added) Use of a microparticle composition of claim 80 for a vaccine.
85. (Newly added) Use of a microparticle composition of claim 80 for raising an immune response.
86. (Newly added) A microparticle composition comprising a microparticle of claim 61 and a pharmaceutically acceptable excipient.
87. (Newly added) The microparticle composition claim 86, wherein said microparticle composition is an injectable composition.
88. (Newly added) A method of delivering a therapeutically effective amount of an immunological adjuvant to a vertebrate subject comprising the step of administering to the vertebrate subject a microparticle composition of claim 86.
89. (Newly added) Use of a microparticle composition of claim 86 for treatment of a disease.
90. (Newly added) Use of a microparticle composition of claim 86 for a vaccine.
91. (Newly added) Use of a microparticle composition of claim 86 for raising an immune response.

REMARKS

Status of the Claims

Claims 1-4, 6-9, 11-14, 17-26, 28-35, 38, 40-42 and 52-91 are pending herein. Claims 5, 10, 15, 16, 27, 36, 37, 39 and 43-51 have been deleted without prejudice or disclaimer and claims 52-91 have been added.

Support for the subject matter of the new and amended claims is generally found in the originally filed claims. For example:

Support for a biodegradable polymer, can be found, for example, in originally filed claim 43.

Support for a cationic or anionic detergent, can be found, for example, in originally filed claims 5 and 6.

Support for an adsorbed adjuvant and an adsorbed antigen can be found, for example, in originally filed claim 2.

Support for an encapsulated adjuvant and an encapsulated antigen can be found, for example, in originally filed claim 3.

Support for a biodegradable polymer is selected from a poly(α -hydroxy acid), a polyhydroxy butyric acid, a polycaprolactone, a polyorthoester, a polyanhydride, and a polycyanoacrylate can be found in originally filed claim 1.

Support for a microparticle composition comprising a pharmaceutically acceptable excipient can be found, for example, in originally filed claim 13.

Support for the claimed emulsion process, including support for a water-in-oil-in-water emulsion process, can be found, for example, in originally filed claim 27 and in the specification at p. 18, lines 10 *et seq.*

Support for immunostimulating nucleotide sequences such as a CpG oligonucleotide; an *E. coli* heat-labile toxin; and a monophosphorylipid A compound can be found, for example, in the specification at page 21, lines 4, 12-13 and 18.

Support for an antigen derived from a pathogenic organism or a tumor can be found throughout the specification. See, e.g., page 13, lines 22-26 and p. 10, lines 7-8. Note that the term "antigen" includes *inter alia*: (a) antigens containing polypeptides (for instance, proteins and glycoproteins--see, e.g., p. 9, lines 13 *et seq.*; see also, e.g., p. 13, lines 22 *et seq.* and